A high-resolution map of the three-dimensional chromatin interactome in human cells.

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Public Summary:

Scientific Abstract:
A large number of cis-regulatory sequences have been annotated in the human genome, but defining their target genes remains a challenge. One strategy is to identify the long-range looping interactions at these elements with the use of chromosome conformation capture (3C)-based techniques. However, previous studies lack either the resolution or coverage to permit a whole-genome, unbiased view of chromatin interactions. Here we report a comprehensive chromatin interaction map generated in human fibroblasts using a genome-wide 3C analysis method (Hi-C). We determined over one million long-range chromatin interactions at 5-10-kb resolution, and uncovered general principles of chromatin organization at different types of genomic features. We also characterized the dynamics of promoter-enhancer contacts after TNF-alpha signalling in these cells. Unexpectedly, we found that TNF-alpha-responsive enhancers are already in contact with their target promoters before signalling. Such pre-existing chromatin looping, which also exists in other cell types with different extracellular signalling, is a strong predictor of gene induction. Our observations suggest that the three-dimensional chromatin landscape, once established in a particular cell type, is relatively stable and could influence the selection or activation of target genes by a ubiquitous transcription activator in a cell-specific manner.